Medical Journal of Europe

ISSN: 2995-7907 doi: 10.5281/zenodo.10702088

Selenium and Antioxidant Effect in Preterm

Nur Aycan [1], Derya Çay Demir [2]

[1] Department of Pediatrics, Yuzuncu Yil University, Faculty of Medicine, Van, Türkiye
[2] Department of Chemistry, Yuzuncu Yil University, Faculty of Science, Van, Türkiye

Article Info

Received: 22 February 2024

Accepted: 25 February 2024

Revised: 25 February 2024

Published: 25 February 2024

Keywords:

Selenium, preterm and antioxidant.

Corresponding author:

Nur Aycan,

Department of Pediatrics, Yuzuncu Yil University, Faculty of Medicine, Van, Türkiye.

drnaycan@gmail.com

This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)

ABSTRACT

Premature babies are deficient in macro and micronutrients at birth. The effect of selenium, an essential factor for the growth and function of vital organs, must be taken into account as much as other nutrients. The optimal dose and length of selenium supplementation have not yet been fully established, as these may vary according to age group and selenium intake in exclusively breastfed children. The clinical situation of infants affected by conditions that may increase oxidative stress and thus increase selenium requirements should be taken into account. Nutritional assessment of Selenium status in the body should be performed to analyze biochemical indicators and clinical signs, especially in premature newborns who are not breastfed.

Cite as: Aycan N, Çay Demir D. Selenium and Antioxidant Effect in Preterm. Med J Eur. 2024;2(2):54-58. doi: 10.5281/zenodo.10702088

INTRODUCTION

Selenium (Se), the thirty-fourth element of the periodic table, was initially misidentified as tellurium by MH Klaproth and later discovered by Swedish chemist JJ Berzelius in 1818. He named it selenium after the Greek goddess of the Moon, Selene (1-3). Selenium is a trace element with antioxidant properties that is considered crucial because of its involvement in major metabolic roles, the immune system, neoplasms, infertility, thyroid hormone metabolism, cardiovascular diseases and neurodevelopmental cascades (4,5). Originally considered a toxin, the trace element selenium is now recognized as an essential micronutrient (6).

Selenium aids in boosting the body's antioxidant defense system by utilizing glutathione peroxidase, a crucial enzyme that aids in neutralizing free radicals and preventing oxidative harm. (7). A group of scientists have discovered that selenocysteine (Sec), an amino acid that contains selenium, is the dominant form of selenium within cells. The protein known as selenoprotein, which contains Sec, is primarily responsible for the beneficial impact of selenium on the body (8). Nevertheless selenoproteins are commonly distributed in several varies, the distribution of selenoproteins variates considerably between varieties. In the human genome, 25 genes encoding selenoproteins have been mapped. Most selenoproteins, including thioredoxin reductases (TrxR), glutathione peroxidases (GPx), and iodothyronine deiodinases (DIO) have well-chactetrized oxidoreductase roles that play an essential function in avoiding oxidative damage as intracellular antioxidants (9,10). Morever, a number of selenoproteins such as selenoprotein K (SELK), selenoprotein N (SELN), selenoprotein S (SELS), selenoprotein M (SELM), selenoprotein F (SEP15), and selenoprotein T (SELT), are considered to be in the endoplasmic reticulum; redox sensing and regulation, unfolded protein response, and calcium homeostasis are all part of their responsibilities. (11). Selenoprotein H (SELH), selenoprotein W (SELW) selenoprotein P (SEPP1), SEP15, SELT, and selenoproteinand

M (SELM) have thioredoxin-like domains, proposing potential redox-related functions (8). Furthermore, biological processes and diverse molecular pathways are attributed to selenoproteins, particularly in the realm of oxidoreductase activities (8,12).

As a result of multiple studies with humans, the absorption of selenium, which has very wide toxic and deficiency dose ranges, varies according to its chemical forms; it is 90% in the case of selenomethionine and 80% in selenite. Selenium is essentially absorbed from the duodenum by enterocytes via amino acid transport facilities and catabolized to elemental selenium, which is incorporated into glutathione peroxidase (2,6).

It has been shown by many studies to play a role in the pathogenesis of non-alcoholic fatty liver disease, Type 2 diabetes, fertility problems, aging, central nervous system diseases, cancer and chronic metabolic diseases (2,10,13-19). Some of the symptoms associated with Se deficiency have been reported as myocardial disorders, skeletal muscle disorders, erythrocyte macrocytosis, nail bed abnormalities, immune system problems, pseudoalbinism and hair loss (16,20). The main sources of selenium in the human diet include garlic, broccoli, bananas, egg yolks, red meat, beef liver, seafood such as salmon, shrimp and tuna, Brazil nuts, Shitaki mushrooms, cottage cheese and whole grain products (13,19).

During a prospective observational study in a pediatric intensive care unit in Brazil, it was determined that higher levels of plasma Se from admission to day 5 were connected to a decrease in ventilation duration and total length of stay (21). Low plasma selenium concentrations are widespread in critically ill patients. However, it is not clear to what extent they reflect deficiency or systemic inflammation. Another study in childhood reported that erythrocyte selenium levels, in contrast to plasma selenium levels, did not change in infants hildren with an acute systemic inflammatory response and that this was related with selenoprotein P. Erythrocyte selenium concentrations as a reliable indicator of selenium status during systemic inflammation may be helpful in critically ill children in specifying whether to rise the selenium dose (22).

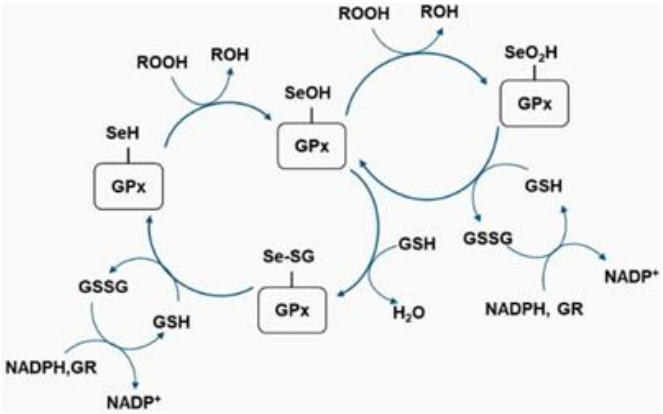

Figure 1. GPx and Se catalytic redox reaction: GSH: glutathione (reduced); GR: glutathione reductase; GSSG: glutathione disulfide; GPx-SeSG: selenenynyl sulfide; GPx-SeOH: selenenic acid; GPx-SeO2H: seleninic acid; ROH: H2O or alcohol; ROOH, hydroperoxide (H2O2, peroxynitrite/aliphatic hydroperoxide); NADPH, Nicotinamide adenine dinucleotide phosphate (46).

PREMATURITY AND SELENIUM

Selenium is carried across the placenta by passive diffusion along a concentration gradient (23). It is especially well preserved in the brain even in the presence of a low nutrient supply (13). It has long been recognized that oxygen free radicals underlie a variety of multifactorial diseases of newborns. These include necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), periventricular leukomalacia (PVL), and neuronal damage in hypoxic ischemic encephalopathy (HIE). Premature newborns have inadequate antioxidant capacity due to both the interruption of antioxidant molecules between the placenta and fetus and inadequate endogenous production (24).

With advancing technology, improved care strategies and trained personnel, more preterm babies all over the world are surviving even if they are born at lower gestational weeks. Babies born at very low gestational weeks are at higher risk for complications associated with prematurity. The combination of early exposure to inflammation following hyperoxia, the consequences of these exposures include an increase in reactive oxygen species and underdeveloped antioxidant defenses, which are believed to play a role in the development of morbidities commonly seen in extreme prematurity. Although Se deficiency alone is unlikely to fully explain free radical damage and oxidant stress in the preterm newborn, sufficient. Se levels potentiate endogenous antioxidant defenses to alleviate the effects of oxidant stress and reduce the accountability of morbidity related with prematurity in theory (5).

The pediatric population, especially premature babies, is known to be sensitive to low Se concentrations due to dietary alteration (4,25). In childhood, selenium deficiency, especially in preterm infants, is closely related to the clinical condition of the patient, the nutritional process after birth and the gestational age at birth (4). Makhoul et al. 2004, investigated selenium levels in cord blood and mothers of 165 preterm and term infants between 24-42 gestational weeks and found that Se concentrations increased with increasing gestational age after 36 weeks of gestation and a linear relationship was found between umbilical cord Se levels, birth weight gestational age, and 5th minute Apgar score (26). Lockitch et al. also found that plasma selenium and glutathione peroxidase levels showed a high correlation with birth week (27). Selenium levels in maternal blood decrease during pregnancy, reflecting the fact that more selenium is transported to the fetus during the third trimester of pregnancy (4). Because Se concentrations in plasma are lower in preterms compared with term infants, accumulation of intrauterine Se stores occurs mainly in the third trimester in preterms (28). Umbilical cord Se levels are approximately 60-75% of maternal plasma Se levels, and cord blood levels are significantly lower in preterms than in term infants (29,30). Numerous studies have shown that parenteral nutrition and formula feeding compared to breastfeeding in the first weeks and months of life are associated with lower and declining Se status in preterm newborns (26,31,32).

Yang et al. declared that both very low and high levels of selenium in cord blood have affects on the neurodevelopment of the child in a negative way conducted a study on prenatal

selenium levels, neonatal cerebellum measurements, and neurodevelopmental assessment of children at 18 months of age with the Bayley-III test (33). In their study, selenium levels in maternal blood were negatively correlated with selenium length in the girl group, while selenium levels in cord blood were correlated with cerebellum width in a positive way (34). Polanska et al. and Skräder et al. also promised that increases in maternal selenium level were followed by improvements in infants' cognitive and motor abilities (35,36). However, Oken et al. has shown that no participation between high levels of erythrocyte-Se during pregnancy and cognitive functioning at school age (median age 7.7 years) (37). Morever, Skräder et al. declared a positive association between maternal erythrocyte-Se levels in early pregnancy and their children's neurodevelopmental test results at age 10 (38).

The Cochrane 2003 report on Se and preterm infants, which included babies with birth weight <2000 grams, proposed that low plasma Se was related to rised risk of complications of prematurity, including BPD, rised days of oxygen dependence and adverse respiratory outcomes. With regard to Se supplementation, a meta-analysis showed that Se supplementation in very preterm babies decreased attacks of late-onset sepsis, but not BPD (7). Se supplementation in very low birth weight infants two decades ago was not associated with improvement in neonatal respiratory outcomes. However, low maternal and infant SE levels before randomization were associated with an increased risk of oxygen dependence at 28 days (39) Winterbourn et al. showed that Se supplementation (7 µg/kg/day and 5 µg/kg/day sodium selenite in parenteral and oral nutrition, respectively) had no effect on oxidative stress, resulting in an almost doubling of selenium levels, but no significant difference in protein carbonyls and the lipid peroxidation product malondialdehyde between groups receiving and not receiving Se supplementation (40).

A multi-country study showed that selenium not only affects preterm infants, but also that selenium levels in pregnant women can vary geographically and trigger preterm births (41). Yang et al. examined trace elements in preterm infants with retinopathy of prematurity and reported that serum selenium levels were much lower than in the control group babies (42). In a study on Se and selenium supplementation in very low birth weight infants, Aggarwal et al. found that daily 10 microgram Se supplementation in very low birth weight infants did not improve the outcome of retinopathy due to prematurity, but the rate of late-onset sepsis, both suspected and culture-proven, was significantly lower than in the placebo group (43).

There is no data are available for the growing population of infants resuscitated at 22-23 weeks' gestation or with a birth weight of less than 500 grams at that time. As of 2015, for preterm infants who are stable and growing the American Society for Clinical Nutrition (ASCN) suggests parenteral Se intake of 2 µg/kg/day and the American Academy of Pediatrics Committee on Nutrition recommends enteral Se intake of 1.3-4.5 µg/kg/day. These suggestions are based on the trace mineral ingredient of human milk, in utero deposition rates and enteral absorption rates for healthy full-term infants; however, these suggestions have not yet been meticulously analyzed. Se supplementation has been recommended for babies with parenteral needs for more than 2-4 weeks. Recent recommendations suggest that Se should be with the initiation of parenteral nutrition, but the data supporting this perpective is inconclusive (5). According to ASPEN (American Society for Parenteral and Enteral Nutrition), 2 micrograms/kg/day is recommended for preterm infants and there is no distinction in terms of dose between premature and term newborns, healthy and sick newborns, and newborns of appropriate gestational age or low birth weight (44). According to the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPHGAN) 2018 recommendations, Se should be routinely supplemented in parenteral nutrition at a dose of 7 micrograms/kg/day in premature infants and 2-3 µg/kg/day in children up to a maximum dose of 100 micrograms/day. Dietary Se is highly bioavailable with up to 80% intestinal absorption; Se intake in breastfed infants is estimated to be 2.3 µg/kg/day (45).

Based on current evidence, Se supplementation in premature newborns does not appear to have any adverse effects. This indicates that the potential benefits of supplementation are likely greater than any perceived risks of deficiency. The lack of data provides a challenging justification for multicenter studies to sufficiently identify Se status in very preterm infants, provide an understanding of typical nutritional necessities, and quantify the clinical outcomes of Se deficiency and excessive exposure on neonatal outcomes in this high-risk population, and recommend targeted rational supplementation strategies (5).

CONCLUSION

Lack of essential nutrients such as carbohydrates, fat, protein, minerals and vitamins in the early life of preterm babies adversely affects the growth and function of vital organ systems. For that reason, preterm infants need to be provided with all essential nutrients in a timely manner. Blood Se concentrations are decreased in newborns, particularly those with birth weight and low gestational age. Additionally, the lowest Se levels are seen in newborns who are not supplemented and are not breastfed, including newborns without any underlying health problems. Therefore, supplementation is essential to reduce the risks of Se deficiency-related complications in non-breastfed preterm babies and to contribute to healthy growth and development of the infant. Updated suggestions for Se supplements are relative to the intake of selenium by breastfed babies, which appears to meet the requirements of newborns. Studies on this topic are definitely needed to promote Se supplementation in all countries and health services to prevent or reverse Se deficiency and the resulting complications in humans, particularly in neonates.

Conflicts of Interest

There is no conflicts of interest between the authors.

Financial Disclosure

There is no funding for that manuscript.

Authorship

Each contributor have participated sufficiently in the work to take public responsibility for appropriate portions of the content of the manuscript.

REFERENCES

1. Berzelius JJ. Additional observations on lithion and selenium. Ann Philos 1818;11:373–375.
2. Kumar BS, Priyadarsini KI. Selenium nutrition: How important is it?, Biomedicine & Preventive Nutrition. 2014;4(2):333-341. doi: 10.1016/j.bionut.2014.01.006.
3. Kabata-Pendias A. Geochemistry of selenium. J Environ Pathol Toxicol Oncol 1998;17(3–4):173–177.
4. Freitas RG, Nogueira RJ, Antonio MA, Barros-Filho Ade A, Hessel G. Selenium deficiency and the effects of supplementation on preterm infants. Rev Paul Pediatr. 2014;32(1):126-135. doi: 10.1590/s0103-05822014000100019.
5. Tindell R, Tipple T. Selenium: implications for outcomes in extremely preterm infants. J Perinatol. 2018;38(3):197-202. doi: 10.1038/s41372-017-0033-3.
6. Fairweather-Tait SJ, Bao Y, Broadley MR, et al. Selenium in human health and disease. Antioxidants & redox signaling, 2011;14(7):1337–1383. doi: 10.1089/ars.2010.3275
7. Darlow BA, Austin, N. Selenium supplementation to prevent short-term morbidity in preterm neonates. Cochrane Database Syst. Rev. 2003;4: CD003312.
8. Labunskyy VM, Hatfield DL. Gladyshev, VN. Selenoproteins: molecular pathways and physiological roles. Physiological reviews, 2014;94(3):739–777. doi: 10.1152/physrev.00039.2013
9. Tinggi U. Selenium: its role as antioxidant in human health. Environmental Health and Preventive Medicine. 2008;13(2):102–108.
10. Genchi G, Lauria G, Catalano A, Sinicropi MS, Carocci A. Biological Activity of Selenium and Its Impact on Human Health. Int. J. Mol. Sci. 2023;24:2633. doi: 10.3390/ijms24032633
11. Pitts MW, Hoffmann, PR. Endoplasmic reticulum-resident selenoproteins as regulators of calcium signaling and homeostasis. Cell calcium, 2018;70, 76–86. doi: 10.1016/j.ceca.2017.05.001
12. Gladyshev VN, Arnér, ES, Berry MJ, Brigelius-Flohé R, Bruford EA, Burk RF. Selenoprotein Gene Nomenclature. The Journal of biological chemistry. 2016;291(46):24036–24040. doi: 10.1074/jbc.M116.756155
13. Rayman M.P. Selenium and human health. Lancet. 2012;379:1256–1268.
14. Solovyev ND. Importance of selenium and selenoprotein for brain function: From antioxidant protection to neuronal signalling.Journal of Inorganic Biochemistry. 2015;153: 1–12.
15. Prabhu KS, Lei XG. Selenium. Advances in nutrition (Bethesda, Md.). 2016;7(2):415–417. doi: 10.3945/an.115.010785
16. Hossain Z, Qasem WA, Friel JK, Omri A. Effects of Total Enteral Nutrition on Early Growth, Immunity, and Neuronal Development of Preterm Infants. Nutrients. 2021;13(8):2755. doi: 10.3390/nu13082755
17. Dahlen CR, Reynolds LP, Caton JS Selenium supplementation and pregnancy outcomes. Front. Nutr. 2022;9:1011850. doi: 10.3389/fnut.2022.1011850
18. Huang J, Xie L, Song A, Zhang C. Selenium Status and Its Antioxidant Role in Metabolic Diseases. Oxidative medicine and cellular longevity. 2022;7009863. doi: 10.1155/2022/7009863
19. Bjørklund G, Shanaida M, Lysiuk R, et al. Selenium: An Antioxidant with a Critical Role in Anti-Aging. Molecules. 2022;27:6613. doi: 10.3390/molecules27196613
20. Masumoto K, Nagata K, Higashi M. et al. Clinical features of selenium deficiency in infants receiving long-term nutritional support. Nutrition. 2007;23:782–787.
21. Leite H, Noguiera P, Iglesias S. Increased plasma selenium is associated with better outcomes in children with systemic inflammation. nutrition. 2015;485–490.
22. de Almeida CB, Leite HP, Lopes Junior E, Konstantyner T, Franco MDCP. Erythrocyte and plasma selenium in children with acute inflammatory response. J Trace Elem Med Biol. 2022;74:127068. doi:10.1016/j.jtemb.2022.127068
23. Nandakumaran M, Dashti HM, Al-Saleh E, Al-Zaid NS. Transport kinetics of zinc, cooper, selenium, and iron in perfused human placental lobule in vitro. Mol. Cell. Biochem. 2003;252:91–96.
24. Gathwala G, Aggarwal R. Selenium supplementation for the preterm Indian neonate. Indian journal of public health, 2016;60(2):142–144. doi: 10.4103/0019-557X.184571
25. Mentro AM, Smith AM, Moyer-Mileur L. Plasma and erythrocyte selenium and glutathione peroxidase activity in preterm infants at risk for bronchopulmonary dysplasia. Biol Trace Elem Res. 2005;106:97-106.
26. Makhoul IR, Sammour RN, Diamond E, Shohat I, Tamir A, Shamir R. Selenium concentrations in maternal and umbilical cord blood at 24-42 weeks of gestation: basis for optimization of selenium supplementation to premature infants. Clin Nutr 2004;23:373-381.
27. Lockitch G, Jacobson B, Quigley G, Dison P, Pendray M. Selenium deficiency in low birth weight neonates: an unrecognized problem. J Pediatr. 1989;114(5):865–870.
28. Shah MD, Shah SR. Nutrient Deficiencies in the Premature Infant. Pediatr. Clin. N. Am. 2009;56:1069–1083.
29. Galinier A, Périquet B, Lambert W, et al. Reference range for micronutrients and nutritional marker proteins in cord blood of neonates appropriated for gestational ages. Early human development, 2005;81(7):583–593.
30. Sluis KB, Darlow BA, George PM, Mogridge N, Dolamore BA, Winterbourn CC. Selenium and glutathione peroxidase levels in premature infants in a low selenium community (Christchurch, New Zealand). Pediatr Res. 1992;32(2):189–194.
31. Smith AM, Chan GM, Moyer-Mileur LJ, Johnson CE, Gardner BR. Selenium status of preterm infants fed human milk, preterm formula, or selenium-supplemented preterm formula. J Pediatr. 1991;119(3):429–433.
32. Sievers E, Arpe T, Schleyerbach U, Garbe-Schönberg D, Schaub J. Plasma selenium in preterm and term infants during the first 12 months of life. J Trace Elem Med Biol. 2001;14(4):218–222.
33. Yang X, Yu X, Fu H, Li L, Ren T. Different levels of prenatal zinc and Selenium had different effect on neonatal neurobehavioral development. Neurotoxicology. 2013;37:35–39.
34. Močenić I, Kolić I, Nišević JR, et al. Prenatal selenium status, neonatal cerebellum measures and child neurodevelopment at the age of 18 months. Environ Res. 2019;176:108529. doi:10.1016/j.envres.2019.108529
35. Polanska K, Krol A, Sobala W, et al. Selenium status during pregnancy and child psychomotor development-Polish Mother and Child Cohort study. Pediatr. Res. 2016;79:863–869.
36. Skräder HM, Hamadani JD, Tofail F, et. al. Selenium status in pregnancy influences children's cognitive function at 1.5 years of age. Clin. Nutr. 2015;34:923–930.
37. Oken E, Rifas-Shiman SL, Amarasiriwardena C, et al. Maternal prenatal fish consumption and cognition in mid childhood: mercury, fatty acids, and selenium. Neurotoxicol. Teratol. 2016;57:71–78.
38. Skräder H, Kippler M, Tofail F, Vahter M. Early-life selenium status and cognitive function at 5 and 10 Years of age in Bangladeshi children. Environ. Health Perspect. 2017;125:117003.

39. Darlow BA, Winterbourn CC, Inder TE, et al. The effect of selenium supplementation on outcome in very low birth weight infants: A randomized controlled trial. J. Pediatr. 2000;136:473–480.

40. Winterbourn CC, Chan T, Buss IH, Inder TE, Mogridge N, Darlow BA. Protein carbonyls and lipid peroxidation products as oxidation markers in preterm infant plasma: associations with chronic lung disease and retinopathy and effects of selenium supplementation. Pediatr Res. 2000;48:84-90.

41. Monangi N, Xu H, Khanam R, et al. Association of maternal prenatal selenium concentration and preterm birth: a multicountry meta-analysis. BMJ Global Health. 2021;6:e005856. doi:10.1136/bmjgh-2021-005856

42. Yang H, Ding Y, Chen L. Effect of trace elements on retinopathy of prematurity. J Huazhong Univ Sci Technolog Med Sci. 2007;27:590-592.

43. Aggarwal R, Gathwala G, Yadav S, Kumar P. Selenium Supplementation for Prevention of Late-Onset Sepsis in Very Low Birth Weight Preterm Neonates. Journal of tropical pediatrics, 2016;62(3):185–193. doi: 10.1093/tropej/fmv096

44. American Society for Parenteral and Enteral Nutrition Appropriate Dosing for Parenteral Nutrition: ASPEN Recommendations. [(Access date:10 October 2023)]. https://www.nutritioncare.org/uploadedFiles/Documents/Guidelines_and_Clinical_Resources/PN%20Dosing%201-Sheet-Nov%202020-FINAL.pdf

45. Domellöf M, Szitanyi P, Simchowitz V, Franz A, Mimouni F; ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Iron and trace minerals. Clin Nutr. 2018;37 (6 Pt B):2354-2359. doi:10.1016/j.clnu.2018.06.949

46. Zhang Y, Roh YJ, Han SJ, et al. Role of Selenoproteins in Redox Regulation of Signaling and the Antioxidant System: A Review. Antioxidants (Basel, Switzerland). 2020;9(5):383. doi: 10.3390/antiox9050383